

REMARKS

Claims 1-3, 5, and 21-24 and pending in the instant application. Claims 1 and 22 have been amended. Claim 21 has been cancelled. Support for the amendments may be found in the specification on page 3 line 27, page 4 lines 8 and 9, and on page 11, lines 25 and 33.

The issues outstanding in the present application are as follows:

- Claims 1-3, 5, and 21 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.K. Patent Application GB 2 294 692 A, Wong *et al.*
- Claims 1-3, 5, and 21 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.K. Patent Application GB 2 306 485 A, Wong *et al.*
- Claims 1-3, 5, and 21 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,117,661, Wong *et al.*
- Claims 1-3, 5, and 21 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,110,074, Flitsch *et al.*
- Claims 22-24 have been rejected under 35 U.S.C. § 103(a) as allegedly being anticipated by U.K. Patent Application GB 2 294 692 A, Wong *et al.*
- Claims 22-24 have been rejected under 35 U.S.C. § 103(a) as allegedly being anticipated by U.K. Patent Application GB 2 306 485 A, Wong *et al.*
- Claims 22-24 have been rejected under 35 U.S.C. § 103(a) as allegedly being anticipated by U.S. Patent No. 6,117,661, Wong *et al.*
- Claims 22-24 have been rejected under 35 U.S.C. § 103(a) as allegedly being anticipated by U.S. Patent No. 6,100,074, Flitsch *et al.*
- Claims 1-3, and 5 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite.

I. 102, anticipation rejections

The Examiner has rejected claims 1-3, 5, and 21 for allegedly being anticipated by U.K. Patent Application GB 2294692A, U.K. Patent Application GB 2306485A, U.S. Patent No. 6,117,661, and U.S. Patent No. 6,100,074 under 35 U.S.C. § 102. Applicants respectfully traverse.

A proper rejection for anticipation under section 102 requires that "each and every limitation of the claimed invention be disclosed in a single prior art reference." *In re Paulsen*, 30 F.3d 1475, 31 U.S.P.Q. 2d 1671 (Fed. Cir. 1994).

The Examiner alleges that the claims are anticipated by GB A 2294692, GB A 2306485, U.S. Patent No. 6,117,661 and U.S. Patent No. 6,100,074. The Examiner has stated that the above references disclose the oxidation of camphor, and thus anticipate the oxidation of monoterpenes. Claim 1 has been amended to claim oxidation of particular monoterpenes and sesquiterpenes which do not comprise oxygen containing substituents. Camphors comprise a ketone group, which is an oxygen-containing substituent. Thus, as all the limitations of the claimed invention are not taught by the cited references, the claims are not anticipated.

II. 103, obviousness rejections

The Examiner has rejected claims 22-24 as allegedly being obvious over GB A 2294692, GB A 2306485, US Patent No. 6,117,661 and U.S. Patent No. 6,100,074. Applicants respectfully traverse.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

The Examiner alleges that the claims are obvious from the disclosure of GB A 2294692, GB A 2306485, US Patent No. 6,117,661 and U.S. Patent No. 6,100,074. The Examiner maintains that the cited references teach that a wide range of organic substrates may be oxidized by a mutant P450 enzyme. Although these references do mention many alkanes, alkenes and aromatic compounds they do not contain any discussion regarding the oxidation of monoterpenes and sesquiterpenes or any prediction of whether or not a mutant P450 enzyme could oxidize these classes of compounds. The terms "monoterpenes" and "sesquiterpenes" do not appear in the cited references.

It must be borne in mind that much of the data presented in the cited references is for the purpose of demonstrating differences between the mutant and wild-type enzymes. Thus although differences can be seen in spin states between the two types of enzymes when they are contacted with different substrates, whether actual oxidation occurs is not clear from much of the data. NADH turnover is not shown for most substrates, and in particular there is no analysis of oxidation products to show the production of oxidized substrates. Thus it is not clear whether this means that oxidation is not occurring. Whilst the data shown in the cited references (Table 2) may demonstrate differences between the mutant and wild-type enzymes (for example in ability to switch spin states) the references leave the skilled person in doubt as to the actual ability of the mutant P450 enzyme to oxidize many of the listed substrates.

Thus the references cited by the Examiner cannot be interpreted as demonstrating to one with skill in the art that mutant P450 enzyme are able to oxidize a wide range of substrates. In order to do that, the references would need to clearly identify data which represents successful oxidation. This is not done, and in particular the references do not discuss any negative results, i.e. a discussion of substrates that were not oxidized.

Thus the skilled person could only make a limited number of conclusions based on the references cited by the Examiner, these essentially being restricted to the comparison the mutant and wild-type enzyme. Given that the only monoterpene that is mentioned is carvone, the skilled person certainly cannot use the cited references to predict whether or not other monoterpenes will be successfully oxidised by mutant 450 enzymes. No sesquiterpenes are mentioned in the references, and thus the skilled person is provided with no teaching in the

cited references which could be used as the basis of a prediction as to whether sesquiterpenes could be successfully oxidised by mutant P450 enzymes.

The Examiner mentions that isoprene oxidation is disclosed in the cited references. Table 2 shows a very low value for the spin state change which occurs in the presence of isoprene. The skilled person seeing this data would very doubtful as to whether successful oxidation was demonstrated and in particular would not be able to predict whether or not monoterpenes and sesquiterpenes could be oxidised by mutant P450 enzymes.

The claims have been amended to limit them to the oxidation of particular monoterpenes whose oxidation is demonstrated in the Examples of the application (see table 6 on page 47). The claims still refer to the oxidation of sesquiterpenes. The oxidation of a sesquiterpene (valencene) is shown in table 6. In addition the claims now exclude substrates with halogen or oxygen containing substituents. Such substituents could be seen to activate a monoterpene or sesquiterpene, and thus this amendment further distinguishes the claims from the subject matter in the cited references concerning the oxidation of compounds which have a halogen or oxygen containing substituent, such as camphor. The data in table 6 of the application shows that mutant P450 enzymes are able to oxidises monoterpenes and sesquiterpenes which have not been activated by a halogen or oxygen containing substituent. Thus the present claims are not obvious from the cited references.

III. 112, indefiniteness rejection

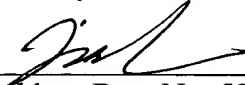
The Examiner has rejected claims 1-3 and 5 under 35 U.S.C. § 112, second paragraph. Applicants respectfully traverse. Claim 1 has been amended to include the SEQ ID numbers of the enzymes indicated. Thus, the rejection is moot, and Applicants respectfully request its withdrawal.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

A check in the amount of \$440.00 is attached to cover the RCE filing fee and a one-month extension of time. Applicant believes no additional fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. HO-P02196US0 from which the undersigned is authorized to draw.

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Respectfully submitted,

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